The Survival Rate Among Unvaccinated, First Dose, and Second Dose Brazilian Hospitalized and ICU COVID Patients by Age Group.

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Abstract. *Brazil has a nationwide surveillance repository of severe acute respiratory disease for hospitalized patients. This repository has stored data for 1,177,151 hospitalized and ICU COVID-19 patients in 2021. In order to statistically validate the difference in the survival rate among unvaccinated, one dose, and two doses, we preprocess the data, divide it into age groups and between hospitalized and ICU patients. This work presents statistical evidence for hospitalized patients that lethality increase with age and decreases with vaccines, especially with the second dose. We found a significant difference among age groups and between hospitalized and ICU, indicating the need to separate these groups when analyzing lethality and comorbidities.*

1. Introduction

The Covid-19 pandemic is completing two years in Brazil, while the beginning of vaccination of the Brazilian population is completing one year. In these two years of the pandemic, we have lived with several variants of the virus, which have changed the dynamics of virus transmission and the occurrence of symptoms in contaminated people. We observe a positive effect of vaccination since the number of deaths has remained stable despite the significant increase in infections.

[Whitaker et al. 2022] and [Estofolete et al. 2022] studied the impact of vaccination considering risk factors which increase the chance of hospitalisation or death with Covid-19. The main risk factors are age, diabetes, asthma, heart disease, kidney disease, liver disease, neurological disease, and immunosuppression. Both studies indicated high vaccine effectiveness in patients within the risk factors group. [Whitaker et al. 2022] analyzed risk factors in England patients grouped by the vaccine (Pfizer Bio N-Tech BNT162b2 and Astra Zeneca AZD1222) and age (16-64, and greater than 64). They pointed out that the results should be interpreted with caution since most patients between the ages of 16 and 64 were not eligible for a second dose in the study period.

[Estofolete et al. 2022] used the Brazilian SIVEP-Gripe database, limiting patients with a diagnosis confirmed via PCR and infected 15 days after vaccination. The data used were restricted to a single hospital between January and September 2021, summing 2,777 hospitalized patients. The results show that the unvaccinated patients have a mean age of 51.08 (±15.56) years, and 71.5% had one or more comorbidities, while

vaccinated patients had an average age of 73.64 (±12.21) years old, and 95.4% had one or more comorbidities. Using regression, they search for predictors of death and find a disassociation between some comorbidities among the vaccinated, while several comorbidities were significant predictors of death in unvaccinated patients. In the vaccinated group, only age +59 and the presence of kidney disorders were predictors of death. They conclude that many comorbidities associated with greater risk in the general population are no longer considered risk factors in vaccinated people.

[Silva et al. 2021] and [Oliveira et al. 2021] also used the SIVEP-Gripe database to analyze COVID-19 in the Brazilian populations but do not consider the vaccination in their studies. [Silva et al. 2021] compares the crude mortality rates from COVID-19 with age-standardized rates in the state capitals and Federal District. This regional and age-adjusted study shows a significant increase in mortality ratio in the north of Brazil compared to the south and south-east. [Oliveira et al. 2021] analyze the risk factors for death among hospitalized children and adolescents, filtering the SIVEP-Gripe database to patients younger than 20 years. They investigate risk factors beyond comorbidities, including socioeconomic, gender, region, and race.

In this context, we present an exploratory study of over 400,000 Brazilian hospitalized patients between January 2021 and December 2021. This study observes the global characteristics of these patients most affected by the virus, analyzes the occurrence of various symptoms in pandemic periods, and creates a statistical profile between the lethality of hospitalized patients vaccinated and unvaccinated. This last analysis considers cohorts as age group, comorbidities, and type of hospitalization (ICU or ward).

The analyses show a considerable difference in the age distribution among vaccinated and unvaccinated, and how lethality increases with age and decreases with vaccines, especially with the second dose. Moreover, there is a significant distinction in vaccine survival effectiveness when comparing hospitalized and ICU. We also explore the comorbidities' presence and lethality by age groups. Lastly, we investigate symptoms variation over time and the symptoms co-occurrence in hospitalized patients.

2. COVID Data

We preprocess and analyze the data available in the SIVEP-Gripe database[1]. This database is a nationwide surveillance repository of patients hospitalized with severe acute respiratory disease in Brazil [OpenDataSUS 2022]. The data in the SIVEP-Gripe is more reliable than the data present in the civil registry and contains more information about the patients [Silva et al. 2021], albeit there are a significant number of sub notification and a lack of standardization on the recording process [Marinho 2021].

Although more reliable than other fonts, the data present in the SIVEP-Gripe database have limitations and characteristics that need to be considered when interpreting and generalizing studies based on its data. The database only records information about hospitalized patients, precluding a safe generalization for milder disease cases. There is a significant difference between official numbers released by the government and those present in the database [Fiocruz 2021a], being more significant in the north and north-east states [Silva et al. 2021]. The media also covered the hospital staff's difficulty using the

[1] https://opendatasus.saude.gov.br/dataset/srag-2021-e-2022

system that feeds the SIVEP-Gripe database, mainly due to lack of time [Globo 2020].

2.1. Preprocessing

The SIVEP-Gripe site makes available a dataset containing all the recorded hospitalized patients with severe acute respiratory disease in Brazil from January 2021 to December 2021. This dataset has 1,702,467 lines (patients) and 83 columns (features). The number of columns increased with time, implying that recent fields have mostly null data. Overall, the columns cover five groups of information: personal (e.g., age, gender, race); regional information (e.g., city, state, hospital name); symptoms (e.g., fever, cough, saturation); comorbidities (e.g., heart disease, pulmonary disease, asthma, kidney disease), and hospitalization (e.g., date evolution (dead or alive), date hospitalization, date of first symptoms, date of vaccines doses).

Since the database record data from severe acute respiratory disease, we maintain only patients hospitalized with COVID-19, reducing the number of lines from 1,702,467 to 1,177,151. We also remove entries without birth date, hospitalization date, evolution date (dead or alive), information about vaccination (yes or no). We also only keep patients infected at least 15 days after vaccination.

While processing the data, we found a group of 24,346 patients whose hospitalize date is previous to the vaccination but was recorded as vaccinated. This group has a normal age distribution and an average lethality of 2.85%, compared to 32.43% found in the unvaccinated group. Considering this anomalous behavior, we also remove this group, ending the preprocessing with a total of 475,152 patients.

Considering that the vaccination in Brazil started on 17 January 2021 and the second dose on 12 February 2021, Figure 1 shows the number of patients hospitalized without the vaccine, with only one dose, and with two doses, grouped by month. Figure 1 offers an overview of the data present in the dataset used in this work. The small number of cases reported in December 2021 is due a "data blackout" caused by hackers that let the recording system offline for weeks [Fiocruz 2021b].

2.2. Age groups

The Brazilian national vaccination plan mainly follows a decreasing age order, implying the need to group the analysis per age group when comparing vaccinated with unvaccinated. Besides, age is the most significant risk factor in hospitalization and death [Whitaker et al. 2022, Estofolete et al. 2022]. Figure 2-A shows the age group distribution from January 2021 to December 2021 for all the unvaccinated patients and Figure 2-B for the patients with at least one dose. The two groups have a distinct distribution. The unvaccinated are more evenly distributed, while vaccinated concentrate most of the patients in age-groups 60, 70, and 80. Considering that the elderly received the vaccines early, we also present Figures 2-C and 2-D, restricting the analysis to August 2021 and forward. In both scenarios, the vaccinated are, on average, 17 years older than the unvaccinated. Comparing the four distributions, we see nuances in the quartiles, but overall, the hospitalized vaccinated are considerably older than hospitalized unvaccinated, following a more uneven distribution. This behavior may indicate that vaccine diminish the chance of younger people being hospitalized.

Figure 1. Dataset entries by month.

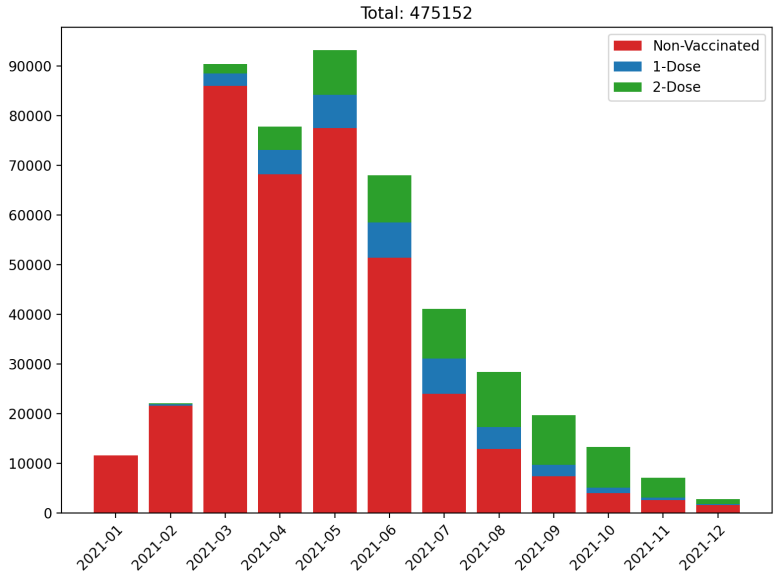
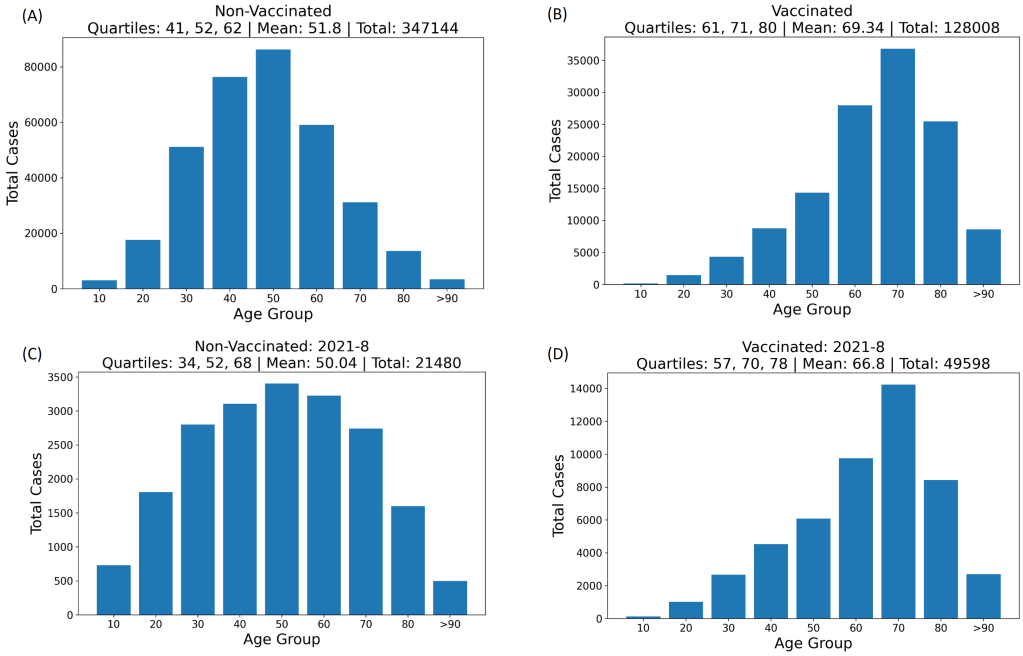


Figure 2. Total cases per age group.



In order to establish statistically significant age groups, we remove patients within the age groups 10 and >90, keeping 454,470 patients on the dataset. Table 1 shows the number of patients per age group by doses and evolution. These groups are the backbone of the following sections, where we explore the comorbidities and lethality among vaccinated and unvaccinated per age group.

3. Comorbidities

Comorbidities increase the chance of hospitalisation or death with Covid-19 [Whitaker et al. 2022]. The SIVEP-Gripe dataset list 13 comorbidities: Asthma, Dia-

Table 1. Number of patients per age group by doses and evolution

Age Group	No Dose Alive	No Dose Deceased	1 Dose Alive	1 Dose Deceased	2 Dose Alive	2 Dose Deceased	Age Group Total
20	15,516	2,455	1,056	121	490	42	19,148
30	43,160	8,946	2,895	484	1,220	158	55,485
40	60,211	18,078	5,581	1,247	2,033	383	85,117
50	60,835	28,208	8,370	3,144	3,023	948	100,557
60	35,271	28,190	14,419	9,210	8,456	4,893	87,090
70	17,394	19,608	16,361	14,603	14,675	12,222	67,966
80	7,156	10,208	9,030	12,713	7,372	9,449	39,107

betes, Down's Syndrome, Heart Disease, Hematological Disorder, Immunocompromise, Kidney disorder, Liver Disorder, Neurological disorder, Obesity, Others Comorbidities, Pneumopathy, Puerperal. Vaccinated people are also known to harbor a greater number of comorbidities than unvaccinated [Estofolete et al. 2022]. In our data, the average number of comorbidities for patients with at least one is 1.6 for unvaccinated and 1.9 for vaccinated. Table 2 shows the percentage of unvaccinated and vaccinated patients with zero, one, two, three, or more than three comorbidities per age group. 64% of the unvaccinated patients in the age group 20 do not have any comorbidities, while in the vaccinated group, the percentage is 51. In all age groups, the percentual of unvaccinated without comorbidities is higher.

Table 2. Percentual number of comorbidities per age group: Unvaccinated — Vaccinated

Age Group	0	1	2	3	4+
20	64% — 51%	27% — 33%	8% — 11%	2% — 3%	0% — 2%
30	66% — 50%	24% — 29%	8% — 15%	2% — 5%	0% — 1%
40	58% — 41%	26% — 31%	11% — 19%	3% — 8%	1% — 2%
50	45% — 28%	30% — 31%	17% — 26%	6% — 11%	1% — 4%
60	32% — 21%	32% — 30%	24% — 30%	9% — 14%	3% — 5%
70	24% — 18%	32% — 30%	28% — 32%	12% — 15%	3% — 6%
80	23% — 17%	33% — 32%	29% — 31%	11% — 15%	4% — 5%

Since hospitalized vaccinated patients have more comorbidities than hospitalized unvaccinated patients, the vaccine may decrease the chance of hospitalization even in the presence of comorbidities. In addition, those vaccinated are more likely to live than unvaccinated, as the next section shows.

4. Lethality Analyses

The death probability of the entire dataset is 35%, which shows how the data in SIVEP-Gripe differs from the vast majority of the COVID-19 cases since it stores data for hospitalized and ICU cases. Adjusting the analysis to unvaccinated, the death probability is 33%, while in the vaccinated group is 40%. The different age distribution explains this contra intuitive finding among the two groups. Table 3 shows the death probability per number of doses among hospitalized and ICU patients grouped by age. The column "Age

Group Total" in Table 3 differ from Table 1 because not all patients had information "yes or no" in the ICU field.

Table 3. Percentual lethality per number of doses among hospitalized and ICU patients

Age Group	No Dose hospitalized	1 Dose hospitalized	2 Dose hospitalized	No Dose ICU	1 Dose ICU	2 Dose ICU	Age Group Total
20	5%	4%	3%	36%	24%	18%	18007
30	7%	5%	4%	41%	31%	28%	52151
40	10%	7%	6%	49%	38%	32%	80175
50	15%	12%	11%	60%	51%	45%	94445
60	25%	20%	18%	71%	63%	60%	81446
70	35%	27%	26%	76%	71%	69%	63434
80	44%	44%	41%	79%	77%	76%	36343

Table 3 shows a clear behavior in all cases: lethality increase with age and decreases with vaccines. Table 3 also demonstrate the importance of separating the lethality analysis in groups as there are significant differences between ages, hospital and ICU, and the number of doses, especially in ICU.

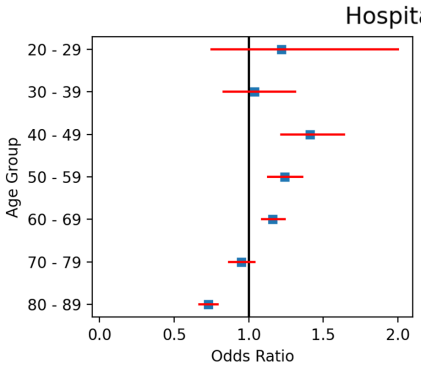
[Whitaker et al. 2022] and [Estofolete et al. 2022] analyze the vaccine effectiveness among individuals in clinical risk groups, dividing patients only into two age groups, older than 60 years and younger. In the current dataset, the death probability for these groups is 25% for unvaccinated under 60 years and 51% for older than 60 years, while in the vaccinated group, these values are 21% and 46%. Although there is a difference among younger and older than 60 years, this analysis does not capture the distinctions present in Table 3.

Considering the disparity between the values of each group presented in Table 1 and to provide a result with statistical significance, we calculated the odds ratio of survival for each age group using confidence intervals and p-values. Since Table 2 shows a significant difference between hospital and ICU, we also present the analyzes regarding this information

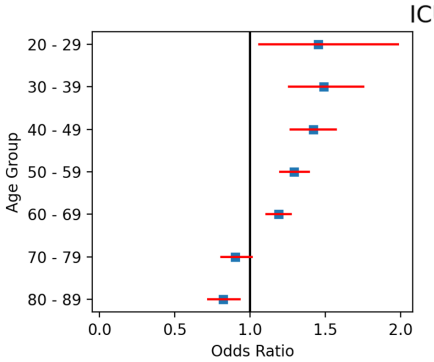
Figure 3 shows the odds ratio of survival for hospitalized and ICU between one dose and unvaccinated. In the 20-29 age groups, from the 411 hospitalized vaccinated patients, 17 died, from the 12,153 hospitalized unvaccinated patients, 610 died. In this case, the odds ratio of survival is $(394/17)/(11,543/610) = 1.22$, meaning the vaccinated have an increased odds of survival of 22%. As the cohort of 411 is small, the odds ratio of 1.22 has a 95% confidence interval of 0.75 to 2. Figure 3 presents this information using a forest plot, where the blue square is the observed odds ratio and the red line is the confidence interval, and a table containing the p-value and the upper (U95) and lower (L95) confidence interval.

For the hospitalized patients, the age groups 20, 30, and 70 do not show a statistically significant difference in the survival ratio between vaccinated and unvaccinated, while in the age group 80, there is a lethality increase among vaccinated. The explanation may lay in the higher number of comorbidities found in the vaccinated group, as shown in Table 2. There is an increase in the survival rate and statistical significance among age

Figure 3. Odds Ratio of Survival for Hospitalized and ICU: One Dose and Unvaccinated.



Age Group	Odds Ratio	p-value	L95	U95
20	1.22	0.249	0.75	2.00
30	1.04	0.389	0.83	1.31
40	1.41	0.000	1.22	1.64
50	1.24	0.000	1.13	1.36
60	1.16	0.000	1.09	1.24
70	0.95	0.147	0.87	1.04
80	0.73	0.000	0.67	0.79



Age Group	Odds Ratio	p-value	L95	U95
20	1.45	0.011	1.06	1.98
30	1.49	0.000	1.26	1.75
40	1.42	0.000	1.27	1.57
50	1.29	0.000	1.20	1.39
60	1.19	0.000	1.11	1.27
70	0.90	0.041	0.81	1.01
80	0.82	0.001	0.72	0.93

groups 20, 30, 40, 50, 60 in ICU compared with hospitalized. Figure 4 presents the same analysis but compares the survival odds between vaccinated patients with the second dose and unvaccinated.

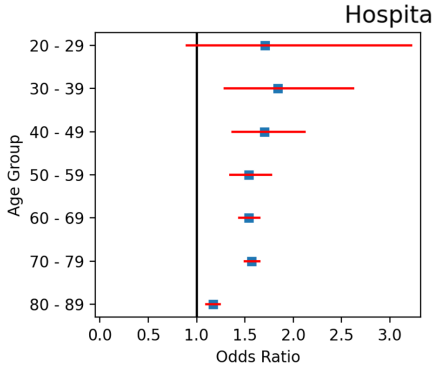
Comparing the results in Figure 3 and Figure 4 there is an increase in the survival rate and statistical significance in all age groups. The second dose enhances survivability, especially in age groups 70 and 80.

Table 4 summarizes the values present in Figure 3 and 4. Values with a p-value greater than 0.05 are crossed out. Overall, vaccines increase the odds of survival, mainly in ICU, and the second dose improve the results over the first dose.

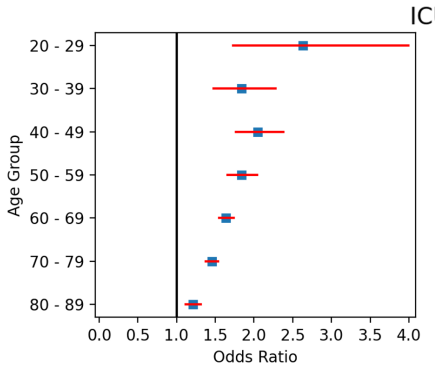
Table 4. Summary - Survival Rate per Age Group: Vaccinated and Unvaccinated

Age Group	1 Dose Hospitalized	1 Dose ICU	2 Dose Hospitalized	2 Dose ICU
20	~~1.22~~	1.45	~~1.71~~	2.63
30	~~1.04~~	1.49	1.84	1.84
40	1.41	1.42	1.70	2.05
50	1.24	1.29	1.54	1.84
60	1.16	1.19	1.54	1.64
70	~~0.95~~	~~0.90~~	1.57	1.46
80	0.73	0.82	1.17	1.21

Figure 4. Odds Ratio of Survival for Hospitalized and ICU: Two Dose and Unvaccinated.



Age Group	Odds Ratio	p-value	L95	U95
20	1.71	0.054	0.90	3.22
30	1.84	0.000	1.29	2.62
40	1.70	0.000	1.37	2.12
50	1.54	0.000	1.35	1.77
60	1.54	0.000	1.44	1.65
70	1.57	0.000	1.50	1.65
80	1.17	0.000	1.10	1.24



Age Group	Odds Ratio	p-value	L95	U95
20	2.63	0.0	1.73	3.99
30	1.84	0.0	1.48	2.28
40	2.05	0.0	1.77	2.38
50	1.84	0.0	1.66	2.04
60	1.64	0.0	1.55	1.74
70	1.46	0.0	1.38	1.54
80	1.21	0.0	1.12	1.31

4.1. Lethality and Comorbidities

Expanding on the analysis done by [Whitaker et al. 2022] and [Estofolete et al. 2022], we investigate how vaccines increase the odds of survival in the presence of comorbidities in seven age groups. Table 5 presents the odds ratio of survival among vaccinated patients (first or second dose) with comorbidity and unvaccinated patients with the same comorbidity. Values with a p-value greater than 0.01 are not shown.

Among the hospitalized, the vaccine increases the odds of survival by an average of 31% for patients with heart disease in the age groups 30, 40, 50, 60, and 70. For the same age groups, the vaccine increase odds of survival by an average of 43% among obese patients. The vaccine also significantly increases the survival rate in patients in the puerperal period. When analyzing Table 5, it is important to consider Table 2, which shows patients may have concurrent comorbidities.

5. Symptoms

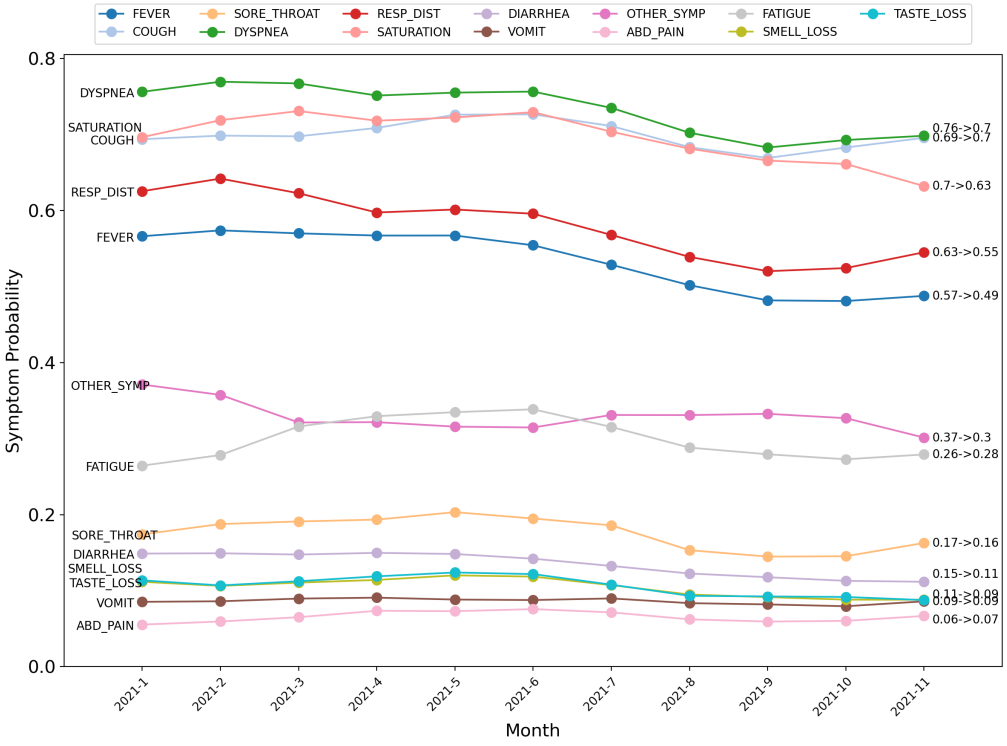
Regarding the occurrence of symptoms, we did not observe significant variations between the symptoms of the vaccinated and unvaccinated, but we did find variations over time. Among hospitalized patients, the symptoms that presented the most variation were fever and respiratory distress, which was more common at the beginning of the pandemic. Unfortunately, the dataset does not present data from patients with mild cases and, therefore, we cannot say whether the same scenario is in cases of non-hospitalization. Figure 5 shows the variation of symptoms over time.

During the months of January to May, fever was present in 57% of hospitalized

Table 5. Survival Rate Among Comorbidities : Vaccinated and Unvaccinated

Comorbidities	Age Group						
	20	30	40	50	60	70	80
Heart Disease	-	1.43	1.36	1.32	1.22	1.23	-
Obesity	-	1.44	1.68	1.37	1.45	1.22	-
Others Comorbidities	1.6	-	1.4	1.19	1.24	1.16	-
Asthma	8.58	-	2.13	1.58	1.51	-	-
Diabetes	-	-	1.4	1.32	1.32	1.23	-
Puerperal	5.4	4.66	-	-	-	-	-
Pneumopathy	-	-	-	-	1.21	-	-
Immunocompromised	-	-	-	-	1.27	-	-
Neurological disorder	-	-	-	-	-	1.37	-
Down's Syndrome	-	-	-	-	-	-	-
Hematological Disorder	-	-	-	-	-	-	-
Kidney disorder	-	-	-	-	-	-	-
Liver Disorder	-	-	-	-	-	-	-

Figure 5. Symptoms of hospitalized patients over time.



patients. From May to September, it drops from 57% to 48%, keeping this value until November. Since fever is an easy measure symptom, it has been widely used as a safety check for COVID-19 in public spaces. Supermarkets, shopping, hospitals, and other places often check the temperature before allowing entrance in Brazil. Given the characteristics of the SIVEP-Gripe data, we can not generalize this result to mild cases,

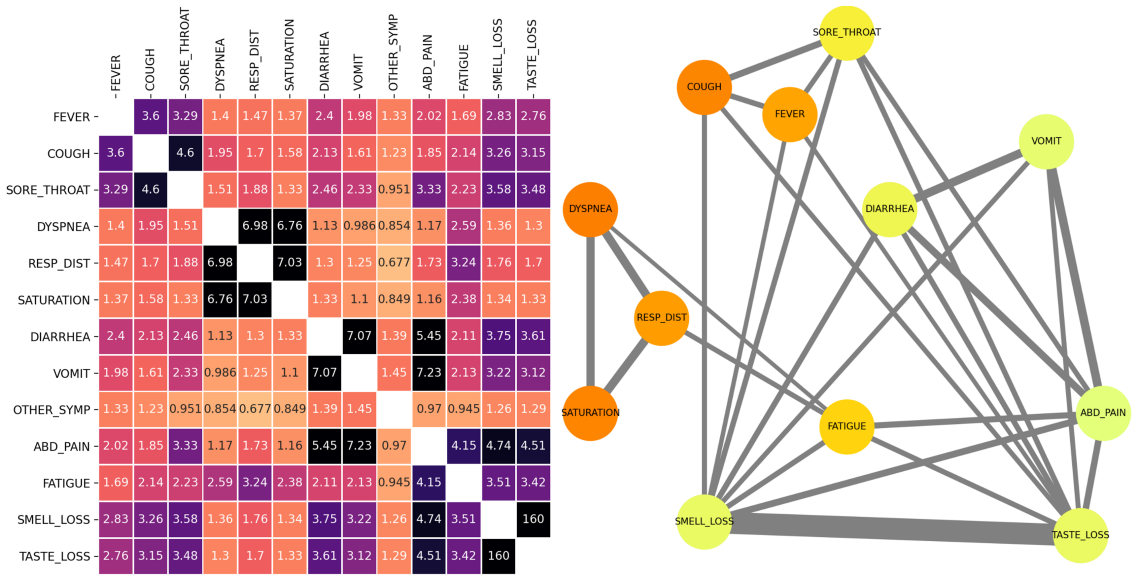
but after September, more than half of the hospitalized patients did not have fever.

5.1. Co-occurrence Between Symptoms

Another point observed in this study is that hospitalized patients present an average of 4.5 different symptoms. These symptoms tend to appear together with a greater chance than simple probability and have a strong association. From the 475,152 patients, 338,931 (71%) had saturation, 354,765 (75%) had dyspnea, and 52,635 (11%) had smell loss. 283,660 patients had both saturation and dyspnea, while 39,049 had both dyspnea and smell loss.

We use a variation of the odds ratio to calculate the strength of co-ocurrance between two symptoms A and B, where is measured the observed intersection against the expected. Following the formula $(both/AnotB)/(BnotA/neither)$, for saturation and dyspnea these values are $((283,660/38,109)/(44,774/40,663)) = 6.76$, and for saturation and smell loss $((39,049/223,159)/(9,802/74,837)) = 1.34$. These results show that saturation is 5 times more associated with dyspnea than with smell loss. Figure 6 shows the this calculation for all pairs of symptoms. Figure 6 also presents a network of symptoms, where the node color indicates its frequency, and the edge thickness the strength of association greater than 2.5.

Figure 6. Strength of Co-occurrence Between Symptoms.



The network in Figure 6 offers better visualization of the values presented in the matrix while keeping only higher associations. Dyspnea, Saturation, and Respiratory Distress often appear together in the patients, in the same way, Vomit, Diarrhea, and Abdominal Pain also do. Smell Loss and Taste Loss are the most associated symptoms. A patient with one of these symptoms will likely have the other.

6. Conclusion, Limitations, and Future Works

The work presents statistical evidence for hospitalized patients that lethality increase with age and decreases with vaccines, specially with the second dose. We found a significant

difference among age groups and between hospitalized and ICU, indicating the need to separate these groups when analyzing lethality and comorbidities.

We did not observe significant variations between the symptoms of the vaccinated and unvaccinated, but we did find some symptoms variations over time. Fever was present in 57% of the hospitalized patients in January 2021, but its presence dropped over time to 48% in November.

Overall, when comparing vaccinated with unvaccinated, we show that vaccinated are on average 17 years older, which may indicate that the vaccine decreases the chance of hospitalization. The vaccine increases the odds of survival between vaccinated and unvaccinated, especially for those in ICU, even though vaccinated patients have more comorbidities.

The database studied, SIVEP-Gripe, has limitations that make this study less complete. The data consider information only from hospitalized patients, making it impossible to analyze patients with mild cases that do not take the hospitalization. Consequently, it is impossible safety generalize the results with less severely ill patients.

Other factors that made the analysis difficult were typing errors, lack of a standard for filling in the information, null fields, and patients whose hospitalization precedes vaccination with very low lethality. Such inconsistencies cast doubt on the credibility of the SIVEP-Gripe, even though several studies.

This work has several extension possibilities. We can replicate the study by separating the data according to the five regions of Brazil, weighting the ages expanding the work of [Silva et al. 2021]. Another possibility is to analyze the efficacy between vaccines types using this dataset, as has been done [Whitaker et al. 2022]. Due to the imbalance and lack of information about vaccines types in the dataset, a solution may be filtering the dataset by hospitals or cities with good release and consistency. Finally, we can also use the symptoms network in a temporal analysis to identify variants.

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